

AMENDMENTS TO THE CLAIMS

1. (Withdrawn) Peptide which is part of the epitope in human IL-15 that is responsible for high-affinity binding of IL-15 to the IL-15Ralpha chain, characterized in that it has the sequence of the region of human mature wild-type IL-15 from L44 to L52 (SEQ ID NO:4), or the sequence of the region of human mature wild-type IL-15 from E64 to I68 (SEQ ID NO:6), or the sequence of the region of human mature wild-type IL-15 from E64 to L69 (SEQ ID NO:67).

2. (Withdrawn) Peptide according to claim 1, characterized in that it has the sequence of the region of human mature wild-type IL-15 from L44 to L52 (SEQ ID NO:4), or the sequence of the region of human mature wild-type IL-15 from E64 to I68 (SEQ ID NO:6)

3. (Withdrawn) Nucleic acid coding for a peptide according to claim 1 or 2.

4. (Currently amended) An IL-15 mutein, characterized in that it has a sequence that is derivable from human mature wild-type IL-15 by ~~at least one substitution, deletion or addition~~ within the region spanning from residue 44 to residue 52, ~~and/or~~ or from residue 64 to residue 68, ~~and/or~~ or from residue 64 to residue 69, this residue numbering corresponding to the human mature wild-type IL-15, provided that the IL-15 mutein resulting therefrom has an affinity for binding to IL-15Ralpha that is either not ~~significantly~~ different from, or higher than the affinity of human mature wild-type IL-15 for binding to IL-15Ralpha.

5. (Currently amended) The IL-15 mutein according to claim 4, characterized in that it has a sequence that is derivable from human mature wild-type IL-15 by ~~at least one substitution, deletion or addition~~ within the region spanning from residue 44 to residue 52, ~~and/or from residue 64 to residue 68~~, this residue numbering corresponding to the human mature wild-type IL-15, provided that the IL-15 mutein resulting therefrom has an affinity for binding to IL-15Ralpha that is either not ~~significantly~~ different from, or higher than the affinity of human mature wild-type IL-15 for binding to IL-15Ralpha, wherein said IL-15 mutein is an IL-15 agonist.

6. (Currently amended) **The** IL-15 mutein according to claim 4 or 5, characterized in that said ~~at least one substitution is a substitution of at least one hydrophobic side chain selected from L, V and I, and/or~~ **or** of ~~at least one non-charged polar side chain selected from S, N, and Q by a charged group selected from D, E, K, and R.~~

7. (Currently amended)] **The** IL-15 mutein according to claim 4 or 5, characterized in that said ~~at least one substitution is a substitution of at least one charged polar side chain selected from E by the oppositely charged group K.~~

8. (Canceled)

9. (Currently amended) **The** IL-15 mutein according to claim [[8]] **4 or 5**, characterized in that said ~~at least one substitution is a substitution of at least one of residues 45, 51, 52.~~

10. (Currently amended) **The** IL-15 mutein according to claim [[9]] **4 or 5**, characterized in that said ~~at least one substitution is a substitution of residue 45 by D or B.~~

11. (Currently amended) **The** IL-15 mutein according to claim [[10]] **4 or 5**, characterized in that it has the sequence of SEQ ID NO:29 or SEQ ID NO:30.

12. (Currently amended) **The** IL-15 mutein according to claim [[9]] **4 or 5**, characterized in that said ~~at least one substitution is a substitution of residue 51 by D.~~

13. (Currently amended) **The** IL-15 mutein according to claim [[12]] **4 or 5**, characterized in that it has the sequence of SEQ ID NO:33.

14. (Currently amended) **The** IL-15 mutein according to claim [[9]] **4 or 5**, characterized in that said ~~at least one substitution is a substitution of residue 52 by D.~~

15. (Currently amended) **The** IL-15 mutein according to claim **[[14]] 4 or 5**, characterized in that it has the sequence of SEQ ID NO:37.

16. (Withdrawn, Currently amended) **The** IL-15 mutein according to ~~claim 4~~ **any one of claims 4-7**, characterized in that it is an IL-15 antagonist **and that it has a sequence that is derivable from human mature wild-type IL-15 by one substitution within the region spanning from residue 64 to residue 69**.

17. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16**, characterized in that said ~~at least~~ one substitution is a substitution of ~~at least~~ one of residues 64, 65, 68.

18. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** **[[17]]**, characterized in that said ~~at least~~ one substitution is a substitution of residue 64 by K.

19. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** **[[18]]**, characterized in that it has the sequence of SEQ ID NO:41.

20. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** **[[17]]**, characterized in that said ~~at least one~~ substitution is a substitution of residue 65 by K.

21. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** **[[20]]**, characterized in that it has the sequence of SEQ ID NO:45.

22. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** **[[17]]**, characterized in that said ~~least one~~ one substitution is a substitution of residue 68 by D.

23. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** [[22]], characterized in that it has the sequence of SEQ ID NO:47.

24. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16**, characterized in that said ~~least one~~ one substitution is a substitution of residue 69.

25. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** 24, ~~characterized in that IL-15 mutein according to claim 24~~, characterized in that said ~~at least~~ one substitution is a substitution of residue 69 by R.

26. (Withdrawn, Currently amended) **The** IL-15 mutein according to claim **4 or 16** [[25]], characterized in that it has the sequence of SEQ ID NO:85.

27. (Currently amended) **A conservative** ~~Conservative~~ fragment of the IL-15 mutein of ~~any one of claims 4-26~~ **claim 4**, which still comprises the mutated 44-52 region and/or mutated 64-68 region and/or mutated 64-69 region, provided that the IL-15 mutein fragment resulting therefrom still has an affinity for binding to IL-15Ralpha that is either not ~~significantly~~ different from, or higher than the affinity of human mature wild-type IL-15 for binding to IL-15Ralpha.

28. (Currently amended) **The** IL-15 mutein fragment according to claim 27, characterized in that it still comprises the mutated 44-52 region ~~and/or mutated 64-68 region~~, provided that the IL-15 mutein fragment resulting therefrom still has an affinity for binding to IL-15Ralpha that is either not ~~significantly~~ different from, or higher than the affinity of human mature wild-type IL-15 for binding to IL-15Ralpha, **wherein said conservative fragment of the IL-15 mutein is an IL-15 agonist.**

29. (Canceled)

30. (Currently amended) The IL-15 mutein fragment according to claim 28 [[29]], characterized in that it comprises the sequence of any one of SEQ ID NO:7-18.

31. (Withdrawn, Currently amended) The IL-15 mutein fragment according to claim 27 ~~or 28~~, characterized in that it is an IL-15 antagonist and that it still comprises the mutated 64-69 region.

32. (Withdrawn, Currently amended) The IL-15 mutein fragment according to claim 31, characterized in that it comprises the sequence of any one of SEQ ID NO: 19-28.

33. (Withdrawn, Currently amended) The IL-15 mutein fragment according to claim 31, characterized in that it comprises the sequence of any one of SEQ ID NO:77-80.

34. (Withdrawn, Currently amended) A nucleic ~~Nucleic~~ acid coding for an IL-15 mutein according to claim 4 ~~any one of claims 4-26~~, or for an IL-15 mutein fragment according to claim 27 ~~any one of claims 27-33~~.

35. (Withdrawn) Vector containing at least one nucleic acid of claim 34.

36. (Withdrawn) Cell transfected or transformed by a vector according to claim 35.

37. (Currently amended) Drug which comprises an IL-15 mutein according to claim 5 ~~any one of claims 8-15~~, and/or an IL-15 mutein fragment according to claim 28 ~~29 or 30~~, and which optionally comprises a pharmaceutically acceptable vehicle and/or carrier and/or diluent and/or adjuvant.

38. (Withdrawn, Currently amended) **A method of treating cancers or immunodeficiency which comprises administering to an individual in need thereof** Use of an IL-15 mutein according to ~~any one of claims 8-15~~ **claim 5**, or [[of]] an IL-15 mutein fragment according to claim 29 or 30, ~~for the manufacture of an anti-cancer or anti-immunodeficiency drug.~~

39. (Withdrawn, Currently amended) **A drug** ~~Drug~~ which comprises an IL-15 mutein according to **claim 16** ~~any one of claims 16-26~~, and/or an IL-15 mutein fragment according to **claim 31** ~~any one of claims 31-33~~, and which optionally comprises a pharmaceutically acceptable vehicle and/or carrier and/or diluent and/or adjuvant.

40. (Withdrawn, Currently amended) **A method of treating inflammation which comprises administering to an individual in need thereof** Use of an IL-15 mutein according to **claim 16** ~~any one of claims 16-26~~, or of an IL-15 mutein fragment according to **claim 31** ~~any one of claims 31-33~~, ~~for the manufacture of an anti-inflammatory drug.~~

41. (Withdrawn, Currently amended) Process for screening for an IL-15 agonist or antagonist, characterized in that it comprises:

- i. providing a plurality of IL-15 muteins according to **claim 4** ~~any one of claims 4-26~~, and/or of IL-15 mutein fragments according to **claim 27** ~~any one of claims 29-35~~,
- ii. comparing their respective binding affinity for IL15-Ralpha to the binding affinity of mature wild-type IL-15,
- iii. selecting those muteins or mutein fragments which have a binding affinity that is not significantly different from, or that is higher than the one of mature wild-type IL-15.

42. (Withdrawn) Process according to claim 41, which is for screening for an IL-15 agonist, characterized in that it further comprises:

iv. selecting at least one detectable IL15-inducible activity, v. comparing the level of said activity that is induced in response to the muteins or fragments selected in step iii., to the one induced by mature wild-type IL-15,

vi. selecting those muteins or fragments which induce an activity level that is not significantly different from, or that is higher than the one of mature wild-type IL-15.

43. (Withdrawn) Process according to claim 41, which is for screening for an IL-15 antagonist, characterized in that it further comprises:

iv. selecting at least one detectable IL15-inducible activity,

v. comparing the level of said activity that is induced in response to the muteins or fragments selected in step iii., to the one induced by mature wild-type IL-15, vi. selecting those muteins or fragments which induce an activity level that is lower than the one of mature wild-type IL-15, or which induce no detectable level of activity.

44. (New) The IL-15 mutein according to claim 4, characterized in that said one substitution is a substitution of one of residues 45, 48, 51, 52, 64, 65, 68 or 69.

45. (New) The IL-15 mutein according to claim 5, characterized in that said one substitution is a substitution of one of residues 45, 48, 51 or 51.